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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/873,555	06/04/2001	Michael Joseph Luzzio	PC10795A	7601

7590 01/22/2004

EXAMINER
LIU, HONG

ART UNIT	PAPER NUMBER
1624	

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DATE MAILED: 01/22/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/873,555	LUZZIO ET AL.	
	Examiner	Art Unit	
	Hong Liu	1624	

-- The MAILING DATE of this communication appears on the cover sh et with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *28 November 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,6-10,12-14,29,34-39,44-49 and 59-68* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,6-10,12-14,29,34-39,44-49 and 59-68* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Claims 1, 6-10, 12-14, 29, 34-39, 44-49, and 59-68 are pending in this application.

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 11/28/03 has been entered.

2.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 6-10, 12-14, 29, 34-39, 44-49, and 59-68 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 59-68 are drawn to a method of treating a hyperproliferative disorder or cancer. These claims are interpreted to include any and all disorders associated with angiogenesis. The specification reads on any and all disorders of cancer or angiogenesis in which cells receive pro-

inflammatory signals through the vascular endothelial growth factor receptor tyrosine kinase. In a recent review article, Carmeliet and Jain discussed the therapeutic perspectives of anti-angiogenic agents in the treatment cancer. The authors pointed out that there are a number of potential problems in the clinical trial of anti-angiogenic agents in the treatment of cancer (Nature, 2000, page 255). The problems include the relevancy of the testing the agent on subcutaneous tumors which are not a common site for human tumors, the distinction of tumor regression and eradication, and the use of agents toxic only to rapidly proliferating cells. There is also uncertainty of long-term side effects of many anti-angiogenic therapies on normal tissues and physiological angiogenesis. The authors concluded that many of these problems can only be addressed with further carefully planned studies. The above discussion makes it clear that, at least as of 2000, much more than routine experimentation would be required to find a compound that will be really effective in treating cancer associated with angiogenesis. As of 2000, there was only the potential, and that success would require future development, i.e. more than routine experimentation. Additionally, no evidence of in vitro/in vivo effectiveness is seen in the specification for one, let alone all, of the instant compounds for the uses claimed herein. See *In re Surrey*, 252 USPQ 724, regarding sufficiency of disclosure. Competent evidence of art-recognized efficacy for intended uses needs to be provided. Any evidence presented must be commensurate in scope with the claims and must clearly demonstrate the likelihood of *in vivo* use for all uses being claimed. See Ex parte Powers, 220 USPQ 925.

Furthermore, the claims embrace the treatment of cancer generally. However, there never has been a compound capable of treating cancer generally. There are compounds that treat some range of cancers, but no one had ever been able to figure out how to get a compound to be

effective against cancer generally, or even a majority of cancers. Thus, the existence of such a "silver bullet" is contrary to our present understanding in oncology. Even the most broadly effective anti-tumor agents are only effective against a small fraction of the vast number of different cancers known. This is true in part because cancers arise from a wide variety of sources, such as viruses (e.g. EBV, HHV-8, and HTLV-1), exposure to chemicals such as tobacco tars, genetic disorders, ionizing radiation, and a wide variety of failures of the body's cell growth regulatory mechanisms. Different types of cancers affect different organs and have different methods of growth and hare to the body, and different vulnerabilities. Thus, it is beyond the skill of oncologists today to get an agent to be effective against cancers generally, evidence that the level of skill in this art is low relative to the difficulty of such a task.

Further, such a term, as set forth in the specification, covers not only all cancers, but also covers any disorders arising from abnormally high rates of proliferation. Thus, it covers precancerous conditions such as different types of abnormal angiogenesis. No agent with anything remotely close to such a scope had ever existed in medicine. When the best efforts have failed to achieve a goal, it is reasonable for the PTO to require evidence that such a goal has been accomplished, *In re Ferens*, 163 USPQ 609. the failure of skilled scientist to achieve a goal is substantial evidence that achieving such a goal is beyond the skill of practitioner in that art, *Genentech vs. Novo Nordisk*, 42 USPQ2nd 1001, 1006.

The word "prodrug" is rejected under 35 U.S.C. 112, first paragraph for reasons already made of record and not withstanding applicants' traverse. Applicants argued that the specification provides definition for "prodrug" on pages 17 and 18 and excerpted the definition of "prodrugs" from pages 17 and 18. However, the definition still could not be found on these

pages. Therefore, the term is still too broad to enable one skilled in the art to determine how the prodrug is converted to active compounds, by what mechanisms and at what site the prodrug will be activated, what in vivo enzymes are likely involved in cleaving the protected group, etc. All these factors are uncertain and require one skilled in the art to spend undue amount of time to practice the invention. For these reasons, the rejection is maintained.

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

The rejection to claims 1-4, 15-18, 30-32, and 40-42 under 35 U.S.C. 112, second paragraph, is maintained for reasons already made of record in the previous office action. For the word "heterocyclic," applicants argue that these terms are defined in the specification and thus definite in light of the specification. However, reading a claim in light of the specification is quite different from reading limitations of the specification into the claim. See In re Prater, 415 F.2nd 1393, 162 USPQ 541. These claims themselves do not carry the limitation as specified in the specification. When the claims having these phrases are given the broadest interpretation, they are still open-ended in terms of the array of heteroatoms, size of the rings, as well as nature of atoms as ring members.

Any inquiry concerning this communication should be directed to Examiner Hong Liu whose telephone number is (703) 306-5814. The examiner can normally be reached on Monday through Friday from 8:30 AM to 6:00 PM.

If attempts to reach the examiner by the phone are unsuccessful, the examiner's supervisor, Mukund Shah can be reached at (703) 308-4716. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 358-1235.

JOHN M. FORD
PRIMARY EXAMINER
GROUP - ART UNIT 1624

Mukund Shah
Supervisory Patent Examiner
Art Unit 1624

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January 12, 2004